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Assessment of the Probability of Autochthonous Transmission of Chikungunya Virus in Canada under Recent and Projected Climate Change

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Background: Chikungunya virus (CHIKV) is a reemerging pathogen transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. The ongoing Caribbean outbreak is of concern due to the potential for infected travelers to spread the virus to countries where vectors are present and the population is susceptible. Although there has been no autochthonous transmission of CHIKV in Canada, there is concern that both *Ae. albopictus* and CHIKV will become established, particularly under projected climate change. We developed risk maps for autochthonous CHIKV transmission in Canada under recent (1981–2010) and projected climate (2011–2040 and 2041–2070).

Methods: The risk for CHIKV transmission was the combination of the climatic suitability for CHIKV transmission potential and the climatic suitability for the presence of *Ae. albopictus*; the former was assessed using a stochastic model to calculate R_0 and the latter was assessed by deriving a suitability indicator (SIG) that captures a set of climatic conditions known to influence the ecology of *Ae. albopictus*. R_0 and SIG were calculated for each grid cell in Canada south of 60°N, for each time period and for two emission scenarios, and combined to produce overall risk categories that were mapped to identify areas suitable for transmission and the duration of transmissibility.

Findings: The risk for autochthonous CHIKV transmission under recent climate is very low with all of Canada classified as unsuitable or rather unsuitable for transmission. Small parts of southern coastal British Columbia become progressively suitable with short-term and long-term projected climate; the duration of potential transmission is limited to 1–2 months of the year.

Interpretation: Although the current risk for autochthonous CHIKV transmission in Canada is very low, our study could be further supported by the routine surveillance of *Ae. albopictus* in areas identified as potentially suitable for transmission given our uncertainty on the current distribution of this species in Canada. https://doi.org/10.1289/EHP669

Introduction

Chikungunya is a reemerging tropical arboviral disease transmitted by *Aedes* (*Ae.*) mosquitoes. Chikungunya virus (CHIKV) was first isolated from human sera and mosquitoes in the Makonde Plateau of the Southern Province of Tanganyika (present day Tanzania) (Robinson 1955; Ross 1956). CHIKV disease is typically characterized by fever, headache, fatigue, and debilitating polyarthralgia and myalgia (Pialoux et al. 2007; Rezza et al. 2007; Robinson 1955). Symptoms generally resolve within 7–10 days with the exception of polyarthralgia that may persist for several months to years (Brighton et al. 1983; Fourie and Morrison 1979; Javelle et al. 2015). Accordingly, the term chikungunya was applied to the disease and roughly translates as "that which bends up" the joints in the local language of the Makonde people (Robinson 1955; Ross 1956). Infrequently, the disease has been suspected to cause complications in severe cases with underlying medical conditions, including death (Economopoulou et al. 2009; Renault et al. 2007). There are no vaccines and treatment is supportive. Asymptomatic cases are rare and clinical manifestations so very characteristic for clinical diagnosis (Ayu et al. 2010; Fourie and Morrison 1979; Higgs and Vanlandingham 2015; Lumsden 1955). Post-infection immunity is life-long (Lumsden 1955; Pialoux et al. 2007).

CHIKV circulates via two distinct transmission cycles: *a*) a sylvatic enzootic cycle transmitted by a wide range of *Aedes* mosquitoes and among wild primate reservoirs in Africa with occasional spillover to humans; and *b*) an urban human–mosquito–human epidemic cycle observed in Asia and the Indian subcontinent (Kendrick et al. 2014) transmitted by two main vectors, *Ae. aegypti* and *Ae. albopictus* (Diallo et al. 1999; Jupp and McIntosh 1988). Until recently, the virus was restricted to Africa, Asia, and the Indian subcontinent where sporadic and isolated outbreaks are reported (Burt et al. 2012; Pialoux et al. 2007; Rougeron et al. 2015; Schwartz and Albert 2010). CHIKV appeared to subside in the 1980s and 1990s only to reemerge in urban outbreaks in Asia and Africa, initiating a large outbreak in 2005–2006 involving millions in the Indian Ocean Islands and southern and central India (Burt et al. 2012; Kalantri et al. 2006; Pialoux et al. 2007; Weaver 2014). The unexpected reemergence of CHIKV in the Indian Ocean region was associated with the mutation of the virus that facilitated virus replication in, and transmission by, *Ae. albopictus* mosquitoes (Thiberville et al. 2013; Tsetsarkin et al. 2007). Consequently, the mutation supported the geographic expansion of CHIKV into sub-Saharan Africa, Southeast Asia, and Europe (Thiberville et al. 2013). Autochthonous outbreaks of CHIKV in Europe were first documented in Italy in 2007 (Rezza et al. 2007), and in France in 2010 (Gould et al. 2010) and 2014 (Delisle et al. 2015). These outbreaks were initiated by infected travelers returning from CHIKV-endemic countries to regions in Europe where *Ae. albopictus* is present (Weaver 2014). More recently, the first cases of autochthonous transmission of CHIKV in the Caribbean were reported in December 2013 on the island of Saint Martin (Pan American Health Organization and World Health Organization 2013). The outbreak has subsequently expanded and is currently

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ongoing with approximately 1.8 million probable and 65,000 confirmed autochthonous cases reported across 47 countries and territories in the Caribbean, Central America, and South America (Pan American Health Organization 2016; Vega-Rúa et al. 2015). Although the outbreak in the Caribbean is caused by an Asian strain that is thought not to be efficiently transmitted by *Ae. albopictus* (Morrison 2014; Weaver 2014), and the principal vector is likely *Ae. aegypti*, there is potential for the spread of imported cases by *Ae. albopictus* (Higgs and Vanlandingham 2015; Vega-Rúa et al. 2015). Associated with the Caribbean outbreak, 11 autochthonous cases of CHIKV were reported in 2014 in Florida where local *Ae. aegypti* and *Ae. albopictus* populations are established (Centers for Disease Control and Prevention 2015; Higgs and Vanlandingham 2015).

To date, there has been no local transmission of CHIKV in Canada due to the absence (to our knowledge) of reproducing populations of *Ae. aegypti and Ae. albopictus*. The cooler Canadian climate is likely a limiting factor for the establishment of these species, particularly *Ae. aegypti*, which is thought to require a tropical or subtropical climate to survive (Christophers 1960). It may be unlikely that *Ae. aegypti* will become established in Canada even if temperatures continue to increase due to climate change (Capinha et al. 2014; Khormi and Kumar 2014). However, *Ae. albopictus* is a cold-tolerant invasive species with the ability to overwinter in a temperate climate (Nicholson et al. 2014), which raises the possibility of the establishment of this species in southern parts of Canada. Occasional *Ae. albopictus* mosquitos have been found in southern Ontario, although these are thought to be "adventitious" individuals rather than evidence of reproducing populations (Giordano et al. 2015; Public Health Ontario 2013). The species is, however, found in the United States where *Ae. albopictus* is thought to be endemic to some southeastern states (Hahn et al. 2016; Kraemer et al. 2015; Ogden et al. 2014; Petersen et al. 2016; Waldock et al. 2013). The rapid rate at which *Ae. albopictus* has spread and established across the United States and parts of Africa and Europe suggests that there is potential for this species to become more widely distributed in the United States and perhaps Canada, particularly under projected climate change (Enserink 2008).

For autochthonous CHIKV transmission to occur in a previously nonendemic location, four conditions must be met: introduction of CHIKV via an infected traveler (condition C1), a susceptible human population (condition C2), climatic suitability for a competent vector (condition C3) and climatic suitability for CHIKV transmission potential by that vector (condition C4) (Ogden et al. 2015). Canada is one of the leading destination countries for travelers returning from CHIKV-endemic countries over the summer months (Khan et al. 2014). In 2014, there were 320 confirmed and 159 probable CHIKV cases returning to Canada, up from 1–20 cases per year in previous years (Drebot et al. 2014; Pan American Health Organization 2016). Because CHIKV infections can cause high viremia and a significant proportion (20%) of infected returned Canadian travelers are viraemic at the time of seeking medical treatment (Drebot et al. 2014), condition C1 is likely currently met although worth noting is that the majority of Canadians travel to CHIKV-affected countries during winter when virus transmission risk is lowest in Canada (Statistics Canada 2016). Although there is no population immunity to CHIKV in Canada, it may be that Canadian residents spend enough of their time during the summer months indoors in air-conditioned buildings and homes that the frequency of mosquito bites is too low to maintain person-to-person transmission. However, the endemic (and sometimes epidemic) transmission of West Nile virus resulting in human cases during the summer months in Canada lends support for the existence of condition C2. Although conditions C1 and C2 are important for autochthonous CHIKV transmission, this study focused on the ecological risk factors essential for endemic CHIKV transmission in Canada (conditions C3 and C4). The current climatic suitability for the presence of *Ae. albopictus* in Canada (condition C3) was identified as unsuitable with the exception for southern coastal British Columbia and in south central and southeastern Canada, but northward expansion is possible with anticipated climate change (Ogden et al. 2014). However, we do not know the current and future climatic suitability for CHIKV transmission in Canada (condition C4), specifically, the effect of temperature on virus survival and replication within mosquitoes, mosquito survival beyond the extrinsic incubation period (EIP) (the time required for the development of CHIKV to spread from the mosquito's gut to the salivary glands where the virus can be transmitted), and virus transmissibility between humans and mosquitoes. In this study we explore the potential for autochthonous, but not necessarily sustained, transmission of CHIKV in Canada. We used a stochastic mathematical model parameterized for *Ae. albopictus* under climatic conditions in the warmest months of the year in locations across Canada. We then combined the climatic suitability for CHIKV transmission potential in the warmest months of the year (condition C4) with climatic suitability indicators for the endemic presence of *Ae. albopictus* (condition C3) to produce risk maps identifying areas in Canada most suitable for autochthonous CHIKV transmission under recent and projected climate.

Methods

Climatic Suitability for Chikungunya Virus Transmission Potential

Transmission potential for CHIKV was explored by modeling the basic reproductive number (R_0) of the virus. We calculated R_0 using a model previously developed for yellow fever and CHIKV that accounts for the temperature-dependent EIP of CHIKV in the vector population and subsequent vector survival beyond the EIP (Johansson et al. 2012; Johansson et al. 2014). In this model, R_0 is the combination of two components, the average number of infectious mosquitoes produced per infectious human, R_0^{HM}, and the average number of infectious humans produced per infectious mosquito, R_0^{MH}:

$$R_0 = R_0^{HM} R_0^{MH}$$

R_0^{HM} is the product of the numbers of mosquitoes per person (φ), the contact rate between humans and mosquitoes (daily biting rate) (α), the probability a mosquito acquires CHIKV from an infectious human during a blood meal (β_{HM}), the duration in days that a human is infectious (V), and the proportion of mosquitoes surviving the EIP (γ):

$$R_0^{HM} = \varphi\alpha\beta_{HM} V\gamma \quad [1]$$

R_0^{MH} is the product of the contact rate between humans and mosquitoes (daily biting rate) (α), the probability a human acquires CHIKV from a feeding infected mosquito (β_{MH}), and the number of days an infectious mosquito survives (L):

$$R_0^{MH} = \alpha\beta_{MH} L \quad [2]$$

The expected number of human infections arising from a single infected human in a completely susceptible population is therefore:

$$R_0 = \varphi \alpha^2 \beta_{HM} \beta_{MH} L V \gamma \quad [3]$$

Table 1 is a summary of the parameters used in the calculation of R_0, which were obtained from a comprehensive scoping review for the parameter values (S. Garasia et al. unpublished data, 2016). The R_0 calculation incorporates three temperature-dependent parameters (φ, L, and γ). A stochastic model was fitted using the parameters summarized in Table 1 to calculate R_0 for the temperature range between 10°C and 40°C. This range captures the temperature range over the summer months (June, July, and August) across Canada when mosquito vectors of CHIKV would most likely be active. To account for uncertainty in the parameters, a total of 50,000 iterations—each sampling from specific distributions for each parameter (Table 1)—was used to calculate R_0. The relationship between temperature and average daily mortality (L) was fitted to a polynomial curve using Matlab R2014a version 8.3. R_0 was calculated using Palisades Corporation @Risk for Excel v6.3.

Figure 1 describes the uncertainty of the parameters on the predicted R_0 between 10°C and 40°C. The mean R_0 values across 50,000 simulations were used to develop cutoffs for risk categories representing the transmission potential for CHIKV, these were *a*) unsuitable when mean $R_0 \leq 0.5$ (corresponding to 10.0°C to <20.3°C and ≥35.7°C), *b*) rather unsuitable when $0.5 <$ mean $R_0 \leq 0.7$ (corresponding to ≥20.3°C to <21.5°C and ≥34.7°C to <35.7°C), *c*) partly suitable when $0.7 <$ mean $R_0 \leq 0.9$ (corresponding to ≥21.5°C to <22.3°C and ≥34.0°C to <34.7°C), *d*) rather suitable when $0.9 <$ mean $R_0 \leq 1.0$ (corresponding to

Table 1. Assumptions, distributions and mathematical equations used to estimate parameters in the calculation of the basic reproductive number (R_0) for CHIKV.

Parameter (*label*)	Description, assumptions, and references	Sampling distribution	Mathematical equation
Daily biting rate (α)	The number of bites on a human, per mosquito, per day. Parameter values for *Ae. albopictus* in other studies include estimates of 0.31 per day observed in Macao, China (Almeida et al. 2005) to a range of 0.19 to 0.39 per day in modeling studies (Christofferson et al. 2014; Manore et al. 2014). We assume a modal value of 0.31 blood meals per day for *Ae. albopictus* in Canada (SD 0.04).	Pert (0.19, 0.31, 0.39)	—
Human-to-mosquito transmissibility (β_{HM})	The probability of a mosquito acquiring CHIKV from an infectious human during a single blood meal. β_{HM} has been estimated to be 0.37 to 0.40 for CHIKV in *Ae. albopictus* (Dumont et al. 2008; Yakob and Clements 2013). Recent changes in the virus indicate β_{HM} may be as high as 0.95 (Dumont et al. 2008). β_{HM} was assumed to have a modal value of 0.40 (SD 0.09).	Pert (0.37, 0.40, 0.95)	—
Mosquito-to-human transmissibility (β_{MH})	The probability of a human acquiring CHIKV from an infected mosquito during a single blood meal. β_{MH} for CHIKV in *Ae. albopictus* has been estimated to range from 0.5 to 0.8 (Dumont et al. 2008). β_{MH} was assumed to have a modal value of 0.65 (SD 0.06) with a lower value of 0.5 and an upper value of 0.8.	Pert (0.5, 0.65, 0.8)	—
Duration of the human infectious period (V)	The period of time in days when infected humans can infect mosquitoes with CHIKV. The viraemic period for CHIKV is up to 8 days, with viral load peaking during the first 3 days of illness and declining from days 4 to 8 (Appassakij et al. 2013). It is also assumed that humans are infectious a day or two prior to becoming ill (Lam et al. 2001; Liumbruno et al. 2008).We assume a mean viraemic period of 6 days (SD 1.1).	Gamma (30, 0.2)	—
Average adult mosquito lifespan in days (L)	The life expectancy of adult *Ae. albopictus* at temperature (T)) is calculated as follows, $L = 1/\mu(T)$ where $\mu(T)$ is defined by a polynomial representing the relationship between temperature and the average daily mortality (Johansson et al. 2014). The following polynomial was fitted to *Ae. albopictus* survival in the field across a temperature range $(0.1 - 33.0°C)$ (Brady 2013; Brady et al. 2013): $\mu(T) = 1.33048 - 2.32772e^{-01}T + 1.68529e^{-02}T^2 - 5.61719e^{-04}T^3 + 7.91643e^{-06}T^4 - 2.72000e^{-08}T^5$ ($R^2 = 0.99$).	-	$L = 1/\mu(T)$
Extrinsic incubation period (EIP)	The mean EIP (EIP_μ) is a function of temperature (T) where: 1. Estimated EIP at 28°C (EIP_{28}) is 6 days (Johansson et al. 2014) 2. Relationship with temperature is assumed to be similar to those of dengue viruses, $\beta_T = -0.08$ (Chan and Johansson 2012; Johansson et al. 2014).	$EIP_{28} = \text{Gamma}\,(9, 0.667)$ $\beta_T = \text{Normal}\,(-0.08, 0.02)$	$EIP_\mu = e^{(\log EIP_{28})e^{\beta_T(T-28)}}$
Proportion of mosquitoes surviving the EIP (γ)	Temperature-dependent *Ae. albopictus* survival is calculated as follows, $\gamma = e^{-EIP/L}$ where $EIP = e^{(\log EIP_{28})e^{\beta_T(T-28)}}$, $L = 1/\mu(T)$ and $\mu(T)$ = fitted polynomial described above (Brady 2013; Brady et al. 2013).	$EIP_{28} = \text{Gamma}\,(9, 0.667)$	$\gamma = e^{-EIP/L}$
Mosquito density per human (φ)	Under ideal weather, mosquito density is proportional to the minimal mortality where L is the temperature-dependent average mosquito lifespan (see formula above) and L_{max} is the maximum mean lifespan; 10.9 days observed at 27°C. In modeling papers, the mosquito density is estimated to be between 1 and 3 mosquitoes per person (Christofferson and Mores 2011; Christofferson et al. 2014; Johansson et al. 2014). We assume for Canada that there are on average two mosquitoes per person under ideal weather conditions (φ_{max}) (SD 0.6).	$\varphi = \text{Gamma}\,(2, 0.4)$	$\varphi = \varphi_{max}\left(\frac{L}{L_{max}}\right)$

Note: SD, standard deviation.

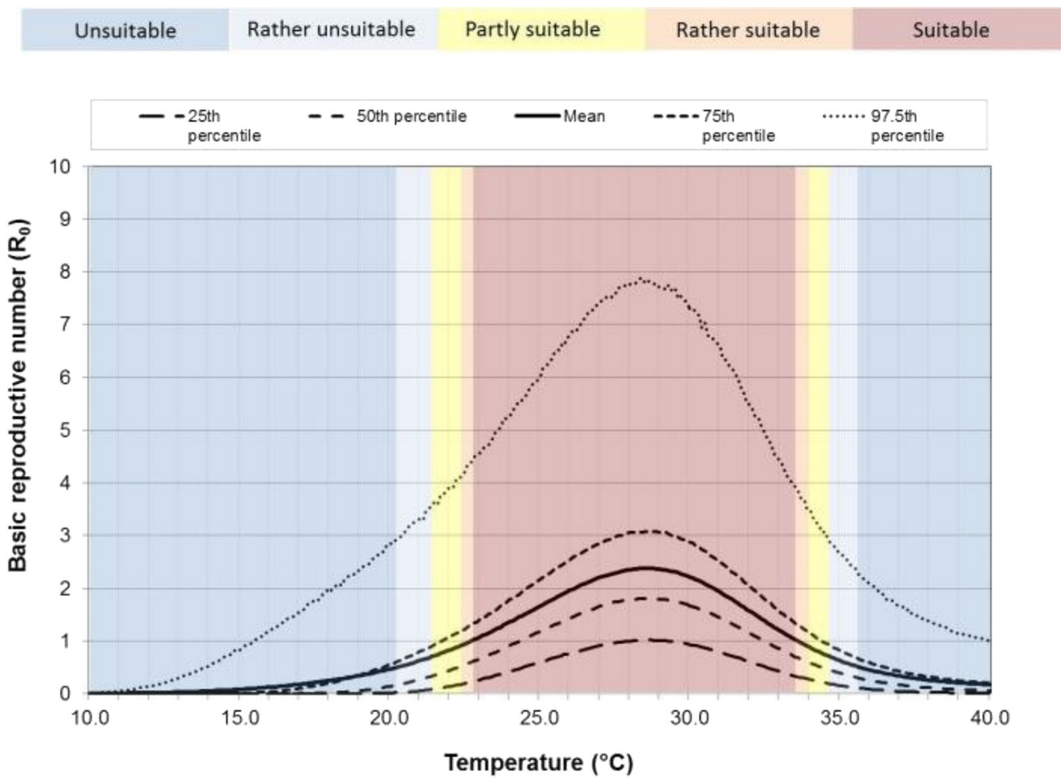

Figure 1. Distribution of R_0 across temperature range at 25th, 50th, 75th, and 97.5th percentiles and the mean. Shaded contours represent corresponding risk categories for the mean R_0 curve representing the climatic suitability for CHIKV transmission potential.

≥22.3°Cto <22.8°C and ≥33.6°C to <34.0°C), and *e*) suitable when mean $R_0 > 1.0$ (corresponding to ≥22.8°C to <33.6°C). The R_0 cutoff values were selected on the assumption that transmission would not be sustainable when $R_0 \leq 0.5$, incrementally sustainable with increasing R_0 values between >0.5 and <1.0, and sustainable when $R_0 > 1.0$ where the virus is expected to spread in a susceptible population. To assign mean R_0 values and risk categories to recent Canadian climate, raw netCDF (network Common Data Form) files containing climate data (ANUSPLIN) derived from the interpolation of daily station-based temperature observations from Environment Canada were obtained for the period 1981–2010 (Hutchinson et al. 2009; McKenney et al. 2011). The gridded observations covered all of Canada south of 60°N on a Lambert conformal conic projection with 5′ arc minutes spacing (equivalent to a horizontal resolution of roughly 10 km).

Mean monthly temperature (T_{mean}) for each year for each grid cell was calculated by averaging the mean daily maximum and mean daily minimum temperatures together. The warmest month of the year was identified for each grid cell and a 5-year moving average was calculated for each grid cell to correct for interannual variability, and an overall mean was calculated for each grid cell representing the mean temperature of the warmest month of the year. A risk category corresponding to the mean temperature of the warmest month of the year was assigned to each 10 km^2 grid cell to reflect the transmission potential for CHIKV under recent climate (Figure 1). The number of months with temperature suitable for CHIKV transmission was also explored, which we considered to be those months with $R_0 > 1.0$ (corresponding to ≥22.8°C to <33.6°C). The climate data were processed using Climate Data Operator (CDO) version 1.6, Max-Planck-Institut für Meteorologie, Germany and NetCDF Operator (NCO) version 4.5 (Zender 2015). ArcGIS®10.3 (Environmental Systems Research Institute [ESRI], Inc.) and Panoply 4.5.0 (National Aeronautics and Space Administration) were used to create temporal-spatial risk maps based solely on mean R_0 values and corresponding risk categories.

Bias Correction of Climate Models

Data from a simulation of one regional climate model (RCM) for the time periods 2011–2040 and 2041–2070 were used to explore CHIKV transmission potential under short-term and long-term projected climate change, respectively. The Canadian Regional Climate Model version 5 (CRCM5) (Hernández-Díaz et al. 2013; Laprise et al. 2013; Martynov et al. 2013; Šeparović et al. 2013) was selected because this RCM has been extensively evaluated over North America. The CRCM5 has shown to have been substantially improved compared to previous Canadian RCMs in terms of seasonal mean statistics for both temperature and precipitation comparable to other modern RCMs (Martynov et al. 2013) and has the greatest skill among other RCMs for simulated precipitation (Diaconescu et al. 2016). The simulations used have horizontal grid meshes of 0.44° (corresponding to approximately 50-km horizontal resolution) and are driven by the recent version of the Environment Canada CCCma (Canadian Centre for Climate modelling and analysis) global climate model (GCM) or global Earth System Model version 2 (CanESM2) (Arora et al. 2011). With the historical period (1961–2005) simulation, two runs were selected per future time period using the Representative Concentration Pathway (RCP, or greenhouse gas emission scenarios) 4.5 and 8.5 (RCP4.5 and RCP8.5), these scenarios represent an intermediate and a high greenhouse gas emission scenario, respectively (van Vuuren et al. 2011).

We used the Linear Scaling (LS) bias correction method (White and Toumi 2013) in order to adjust RCM time series with correction values based on the differences between mean observed (gridded ANUSPLIN) values and RCM simulation. The LS method aims to perfectly match the monthly mean of corrected values with that of observed ones (Lenderink et al. 2007). It operates with monthly correction values based on the differences between observed and raw data (raw RCM simulated data in this case). The LS method was applied to the CRCM5 simulation over the historical period as well as on the RCP4.5 and RCP8.5 future simulations. Comparison between the bias-corrected climate data from the CRCM5 model driven by CanESM2 under RCP4.5 and RCP8.5 and climate data from other RCMs driven by CanESM2 or the Irish Centre for High-End Computing EC Earth climate model (ICHEC-EC-EARTH) under RCP4.5 and RCP8.5 over two time periods (2011–2040 and 2041–2070) across Canada showed that the bias-corrected climate data from CRCM5-CanESM2-RCP4.5 and CRCM5-CanESM2-RCP8.5 used in this study were not far outliers compared to other models and did not deviate significantly from the ensemble mean (see Figure S1). The bias-corrected minimum and maximum temperature for each month and each CRCM5 grid were used to obtain R_0 values for each grid cell for the hottest month of the year, and to calculate the number of months each cell was suitable (if at all) for CHIKV transmission. A risk category corresponding to the mean temperature of the warmest month of the year was assigned to each $50km^2$ grid cell representing the transmission potential for CHIKV under short-term and long-term projected climatic conditions simulated using the two different emission scenarios.

Climatic Suitability for the Presence of Aedes albopictus

We used the linear index of precipitation and air temperature suitability described by a sigmoidal function (SIG) to assess the climatic suitability for *Ae. albopictus*. The SIG index was originally developed to assess the climatic suitability of *Ae. albopictus* in Europe (Caminade et al. 2012; European Center for Disease Prevention and Control 2009) and was found to be a good fit to the current distribution of this species in the United States (Ogden et al. 2014). The SIG index is defined by three components: *a*) January mean temperatures (T_{mean}), *b*) summer mean temperatures (T_{mean} from June to August) and *c*) total annual precipitation; each component is transformed into an interval ranging between 0 and 255 using sigmoidal functions. These three components are then linearly combined using the arithmetic mean and rescaled to a range between 0 and 100 to derive a suitability indicator that captures a set of climatic conditions known to influence the ecology of *Ae. albopictus* as previously described (Caminade et al. 2012). A SIG value was calculated for each grid cell below 60°N covering Canada using observed climate data (ANUSPLIN, over the 1981–2010 period) and bias-corrected projected climate simulated data (CRCM5 under the RCP4.5 and RCP8.5, over the 2011–2040 and 2041–2070 periods). Bias-corrected temperature and precipitation data for each grid cell were detrended over time periods using 5-year moving averages. In the United States, *Ae. albopictus* was not observed below a SIG value of 66.7 (sensitivity of 84.5% and specificity of 92.2%) (Ogden et al. 2014). Accordingly, suitability classes corresponding to SIG values were derived for Canada, these were *a*) unsuitable when SIG < 66.7, *b*) moderate when SIG ≥ 66.7 and SIG < 75, *c*) high when SIG ≥ 75 and SIG < 85, *d*) very high when SIG ≥ 85and SIG < 95, and *e*) totally suitable when SIG ≥ 95. The SIG cutoff values were selected to approximately distribute values from 66.7 to 100 equally across suitability classes on the assumption that SIG ≥ 66.7 is not suitable for *Ae. albopictus*, incrementally suitable with increasing SIG values between 66.7 and <95, and very suitable when SIG ≥ 95. A suitability class corresponding to SIG values was assigned to each grid cell for each of the five climate datasets.

Climatic Suitability for Potential Autochthonous CHIKV Transmission in Canada

The risk categories for CHIKV transmission potential (R_0) were overlain with the SIG suitability classes representing the presence of *Ae. albopictus* to produce overall risk categories that allowed risk maps to be drawn that identify areas in Canada at risk for short-term autochthonous CHIKV transmission under recent and projected climate change. Similar to other studies in Europe (Fischer et al. 2010; Fischer et al. 2013), we assumed that climatic suitability for CHIKV transmission potential in combination with climatic suitability for the presence of *Ae. albopictus* results in higher risk for autochthonous CHIKV transmission via this particular vector. Accordingly, the R_0 values and their corresponding risk categories reflecting the transmission potential for CHIKV for each grid cell (Figure 1) were combined with the SIG values and their corresponding suitability classes reflecting the climatic suitability for *Ae. albopictus* for each grid cell to produce an overall CHIKV suitability risk category (Figure 2). This overall CHIKV suitability risk classification was then assigned to each grid cell in Canada for each of the five climate datasets. ArcGIS®10.3 [Environmental Systems Research Institute (ESRI), Inc.] and Panoply 4.5.0 (National Aeronautics and Space Administration) were used to create temporal-spatial risk maps based on the overall CHIKV suitability risk classification.

Sensitivity Analysis

We assessed the sensitivity of our assessments to the selection of parameter values in the transmission model by mapping the risk for autochthonous CHIKV transmission when using parameter values for the 75th percentile value of R_0 (see Figure S2) rather than mean R_0 (Figure 2).

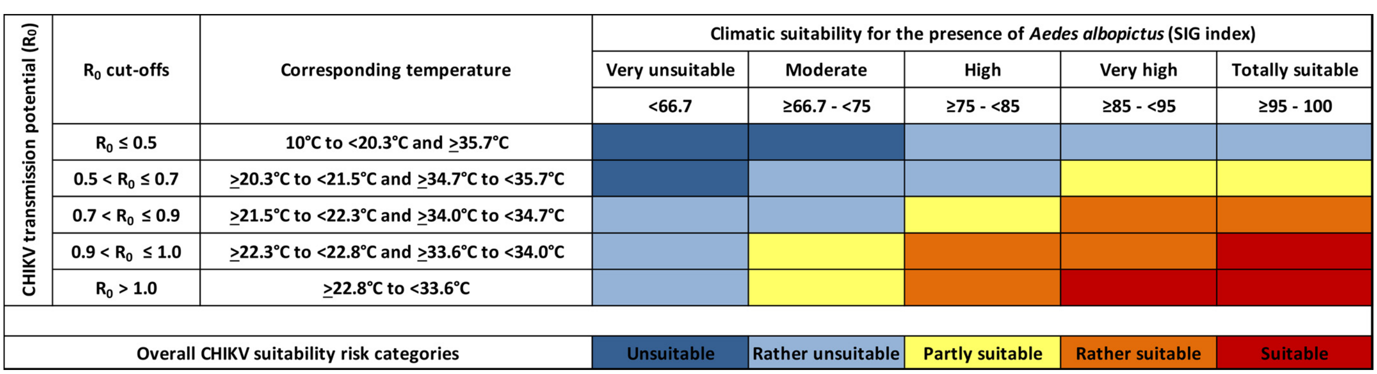

Figure 2. Risk categories for autochthonous CHIKV transmission by *Ae. albopictus* in Canada derived from combining the climatic suitability for CHIKV transmission potential (R_0) with the climatic suitability for the presence of *Ae. albopictus* (SIG index).

Results

Risk Classification for Chikungunya Virus Transmission Potential

Our model of climatic suitability for CHIKV transmission potential indicated optimal suitability when the mean monthly temperature of the warmest month of the year is between $\geq$22.8°C and 33.6°C (R_0> 1.0) (Figure 1). Figure 3 shows the areas in Canada that have at least 1 month in the year where the climate is suitable for autochthonous CHIKV transmission based solely on modeling temperature-dependent R_0 without consideration of the climatic suitability for the presence of *Ae. albopictus*. Under recent climate (observed ANUSPLIN 1981-2010), the majority of Canada does not have 1 month in the year when mean temperature is $\geq$22.8°C and thus is not currently climatically suitable for autochthonous CHIKV transmission. One small area in southern Ontario, where mean summer temperature is $\geq$22.8°C, was suitable but this is limited to only 1 month of the year (July) (Figure 4). Under short-term projected climate (2011–2040) for both RCP4.5 and RCP8.5 scenarios, locations in southern parts of the provinces of Ontario, Québec, British Columbia, and the Canadian Prairies (Alberta, Saskatchewan, and Manitoba) become increasingly favorable for CHIKV transmission based solely on modeling temperature-dependent R_0 (Figure 3), although this is limited to 2 months in the year (July and August) (Figure 4). Under long-term projected climate (2041–2070) for both emission scenarios, further areas across Canada become favorable for CHIKV transmission based solely on modeling temperature-dependent R_0 (Figure 3) and the transmission period expands to 3 months in the year (June to August) (Figure 4). However, the risk maps in Figures 3 and 4 are based solely on R_0 and the recent climate (1980–2010) risk maps are only relevant if vectors competent for transmitting CHIKV other than *Ae. albopictus* exist in Canada given the absence of this vector under the current climate. However, it is possible that *Ae. albopictus* could survive in some of the identified risk areas under short-term (2011–2040) and long-term (2041–2070) projected climate.

When using transmission model parameter values for the 75th percentile value of R_0 rather than mean R_0, a larger area of southern Ontario becomes suitable for transmission ($R_0 > 1.0$) under recent climate but this remains limited to 1 month of the year (July) (see Figure S3). Under RCP4.5 2011–2040, areas suitable for transmission have expanded across southern Ontario and Québec and into British Columbia. Under RCP4.5 2041–2070, larger areas of southern Ontario, Québec, and British Columbia become suitable for transmission, in addition, parts of southern Alberta, Saskatchewan, Manitoba, New Brunswick, Nova Scotia, and western Ontario become suitable for transmission. Under RCP8.5 for both 2011–2040 and 2041–2070, the southern parts of provinces between British Columbia and Québec become suitable for transmission with concentration of suitability expanding significantly in southern Alberta, Saskatchewan, Manitoba and Québec and western and southern Ontario under long-term projected climate. Additional areas in southern New Brunswick and Nova Scotia become suitable under long-term projected climate. No new high risk areas were identified when compared with maps produced using mean R_0 (Figure 3). The time period of possible transmission remains between 2 and 3 months (June to August) under RCP4.5 2011–2040, RCP4.5 2041–2070 and RCP8.5 2011–2040 scenarios but increases to up to 4 months (June to September) under RCP8.5 2041–2070 (see Figure S4).

Risk Classification for Autochthonous Chikungunya Virus Transmission in Canada

When climatic suitability risk categories of CHIKV transmission potential (R_0) were overlain with climatic suitability for the presence of *Ae. albopictus* populations, the risk for autochthonous CHIKV transmission by *Ae. albopictus* under recent climate (1981–2010) was very low with all of Canada classified as

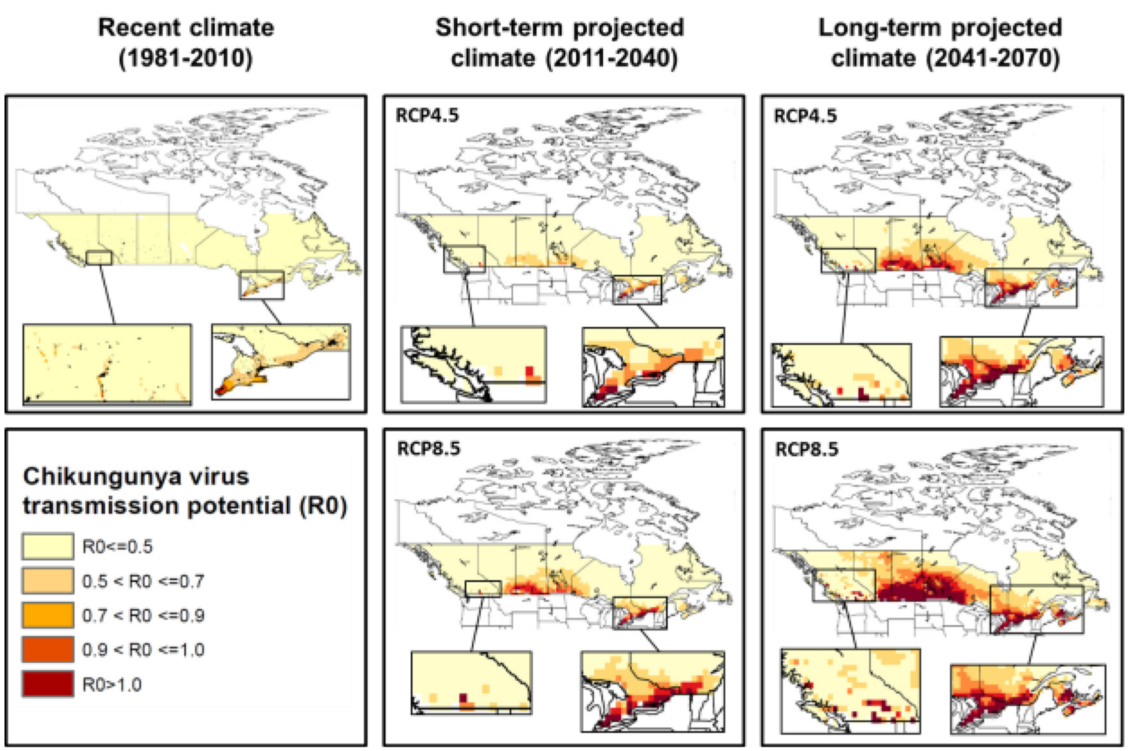

Figure 3. Risk maps for autochthonous CHIKV transmission in Canada based solely on CHIKV transmission potential (R_0); transmission potential represents risk based on having at least 1 month per year with CHIKV transmission potential. Provincial and territorial boundaries of Canada, 2001. Source: © 2003. Government of Canada with permission from Natural Resources Canada.

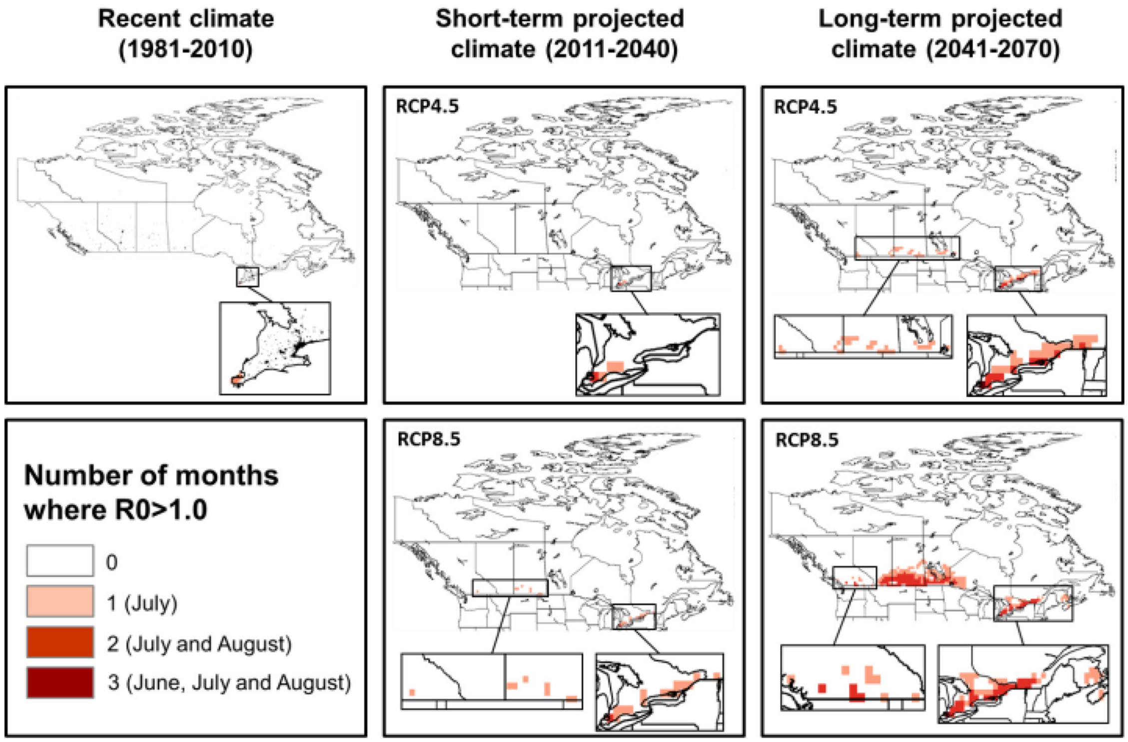

Figure 4. Duration in months where mean $R_0 > 1.0$ (mean monthly temperature between $\geq$22.8°C and 33.6°C) in Canada based solely on CHIKV transmission potential (R_0). Provincial and territorial boundaries of Canada, 2001. Source: © 2003. Government of Canada with permission from Natural Resources Canada.

unsuitable or rather unsuitable for CHIKV transmission (Figure 5). Under short-term projected climate (2011–2040) for both RCP4.5 and RCP8.5 scenarios, a small area of southern coastal British Columbia becomes partly suitable for CHIKV transmission but the rest of Canada remains unsuitable or rather unsuitable for transmission (Figure 5). Under long-term projected climate (2041–2070), for both emission scenarios, an increasingly larger area of southern coastal British Columbia becomes rather suitable or suitable for CHIKV transmission (Figure 5). However, for these areas the duration of climate suitable for potential transmission is limited to 1–2 months in the year (August under RCP4.5 and July–August under RCP8.5) (Figure 6). The rest of Canada remains unsuitable or rather unsuitable for CHIKV transmission under long-term projected climate (2041–2070) (Figure 5). Although the risk maps for transmission based solely on CHIKV transmission potential (R_0) suggests southern Ontario is currently most suitable due to warmer summer temperature (Figure 3), after taking into account climatic requirements for the presence of *Ae. albopictus*, the current climatic suitability for CHIKV transmission via this vector in southern Ontario and the rest of Canada is very low (Figure 5). Therefore, the future climatic suitability for autochthonous CHIKV transmission in Canada via *Ae. albopictus* is expected to be limited to southern coastal British Columbia with possible transmission restricted to 1–2 months in the year (Figures 5 and 6).

The implications of using the 75th percentile value of R_0 rather than the mean R_0 in sensitivity analysis was similar for the R_0 model. Under recent climate, all of Canada remains unsuitable or rather unsuitable for CHIKV transmission (see Figure S5). Under short-term projected climate (2011–2040) for both RCP4.5 and RCP8.5 scenarios, the small area of southern coastal British Columbia that was identified as partly suitable for transmission using mean R_0 has become rather suitable for transmission but the rest of Canada remains unsuitable or rather unsuitable for transmission. Under long-term projected climate (2041–2070), for both emission scenarios, an increasingly larger area of southern coastal British Columbia becomes rather suitable and suitable for transmission; these areas are larger and further north along the coast compared to areas identified as suitable for transmission using mean R_0. The rest of Canada remains unsuitable or rather unsuitable for CHIKV transmission under long-term projected climate. The duration of climate suitable for potential transmission remains limited to 1–2 months of the year (July–August) (see Figure S6) and no new high risk areas were identified.

Discussion

In this study we investigated the climatic suitability for autochthonous CHIKV transmission in Canada. The objective was to quantitatively assess the current and future climatic suitability for CHIKV transmission under two greenhouse gas emissions scenarios (RCP4.5 and RCP8.5) using simulations from RCM to provide insight into where, when and for how long local transmission of CHIKV might occur in Canada. To achieve this, we assessed the climatic suitability for CHIKV transmission potential (R_0) and combined this with the climatic suitability for the presence of *Ae. albopictus* (Ogden et al. 2015), on the assumption that for autochthonous transmission to occur, there must be climatic suitability for both pathogen transmission for a minimum of 1 month, and for the vector over a sustained period (Fischer et al. 2013). Clearly with a minimum EIP duration of approximately 6 days at 28°C for CHIKV (Johansson et al. 2014), autochthonous transmission could occur in locations where temperature conditions suitable for transmission occur for periods shorter than 1 month. However, in Canada, temperatures are not frequently $\geq$28°C for sustained periods. The mean monthly temperature for the warmest month of the year for Canada south of 60°N under recent climate was 15.7°C with a range of 3.5°C to 23.4°C. The

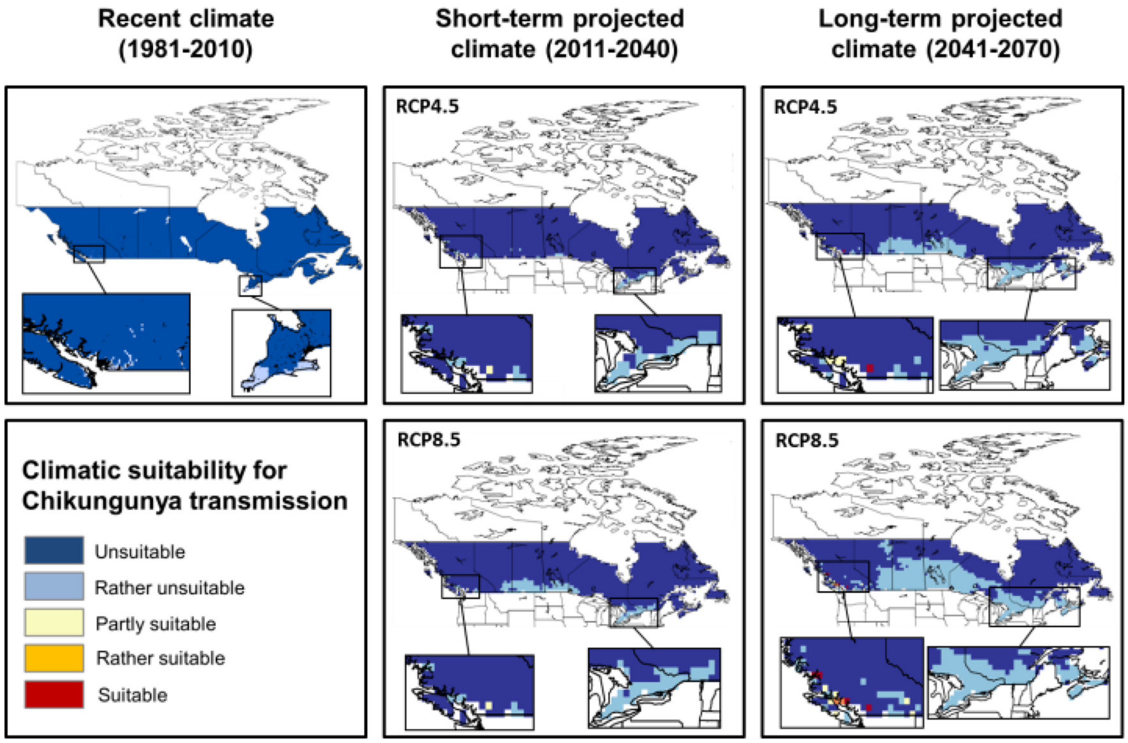

Figure 5. Risk maps for autochthonous CHIKV transmission in Canada combining the climatic suitability for CHIKV transmission potential (R_0) with the climatic suitability for the presence of *Ae. albopictus* (SIG index). Provincial and territorial boundaries of Canada, 2001. Source: © 2003. Government of Canada with permission from Natural Resources Canada.

mean EIP from 50,000 iterations in the R_0 model was approximately 14.4 days when temperature was held at 23.4°C, suggesting monthly values are appropriate to explore the CHIKV transmission cycle period in Canada. There may be a slight underestimate of risk of autochthonous transmission were endemic mosquito species to be competent vectors but as *Ae. albopictus* population persistence depends on year-round temperature conditions it should have a lesser effect on risk of transmission by this species. Most of the areas that were identified as climatically suitable for CHIKV transmission were not suitable for *Ae. albopictus* due to the latter having requirements for generally warmer climate. The climatic suitability for CHIKV transmission potential is driven by temperature, in particular the temperature-dependent EIP of CHIKV in the vector population and vector survival beyond the duration of the EIP (Johansson et al. 2014), while climatic suitability for the presence of *Ae. albopictus* is dependent on bioclimatic conditions that are known to influence the vector's ecology including the ability of eggs to overwinter, precipitation to initiate egg hatching and warm summer temperature for mosquitoes to reach a viable reproducing population over a sustained period for successive transmission cycles (Caminade et al. 2012).

Our study suggests that Canada is currently not climatically suitable for autochthonous CHIKV transmission. Although we have the climatic suitability for limited CHIKV transmission over the summer period, the long and harsh winters impede survival of mosquito eggs and subsequently the establishment of the two known CHIKV vectors, *Ae. aegypti* and *Ae. albopictus*. The former has a minimum egg survival temperature threshold of -2°C, whereas the latter has a threshold of -10°C for exposures over 12 h (Thomas et al. 2012). Because *Ae. albopictus* is more cold tolerant, it is expected that this species would be the one to realistically have a chance of becoming established in Canada, as has occurred in temperate Europe (Delisle et al. 2015; Gould et al. 2010; Rezza et al. 2007). It is likely that our current winter temperature is below the minimum threshold for either *Ae. albopictus* or *Ae. aegypti* to survive and establish in most parts of Canada, which is a hypothesis consistent with studies on these species globally (Bonizzoni et al. 2013; Capinha et al. 2014; Khormi and Kumar 2014; Kraemer et al. 2015; Waldock et al. 2013). Nevertheless, given recent evidence for the survival of these species in urban areas (Lima et al. 2016) and reports of *Ae. albopictus* along the southern shore of Lake Erie, which is geographically close to areas of southern Ontario (Hahn et al. 2016), surveillance to rule out their presence may be prudent.

Our study did identify the potential for parts of southern coastal British Columbia to become progressively suitable for CHIKV transmission under short-term and long-term projected climate, particularly driven by a high emission scenario (RCP8.5). The duration of the transmission season, although short, is expected to expand from 1 month in a very small area in British Columbia in the short-term to 2 months covering a larger area in British Columbia in the long-term. This would be sufficient to sustain short-term autochthonous CHIKV transmission were pathogen and vector to co-occur (Reiskind et al. 2008). *Aedes albopictus* has not been detected in British Columbia although routine surveillance in this province has been sporadic and targeted to *Culex* spp. vectors of West Nile virus (communication, M. Morshed, May 2017, BCCDC). Our findings suggest that CHIKV and mosquito surveillance in the identified risk areas in British Columbia may be prudent, particularly as *Ae. albopictus* has been found in at least one county in the adjacent state of Washington (Hahn et al. 2016). However, if other species of Canadian-endemic mosquitoes turn out to be competent vectors for CHIKV, or if *Ae. albopictus* becomes more adapted to a cooler environment, the area of risk would expand further north and inland than currently expected and surveillance of the pathogen and vector should also be

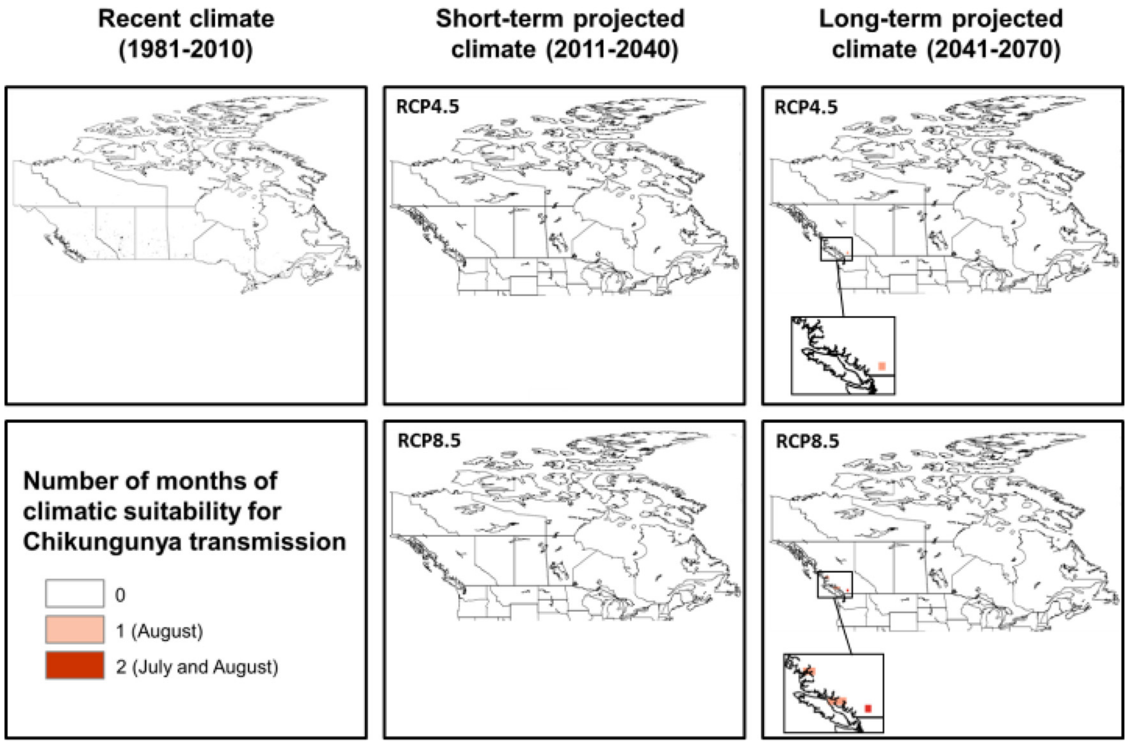

Figure 6. Duration in months for potential autochthonous CHIKV transmission in Canada combining the climatic suitability for CHIKV transmission potential (R_0) with the climatic suitability for the presence of *Ae. albopictus* (SIG index). Provincial and territorial boundaries of Canada, 2001. Source: © 2003. Government of Canada with permission from Natural Resources Canada.

considered in southern Ontario, Québec, and the Canadian Prairies. Worth noting is that our study only considered two greenhouse gas emission scenarios (RCP4.5 and RCP8.5) representing intermediate and high emission scenarios, respectively. Implementation of the recent 2016 Paris Climate Agreement puts Canada on track for the RCP4.5 path, in which case the risk maps for CHIKV transmission under the RCP4.5 scenario would be the most likely projection. Under this scenario, we would expect reduced areas to be suitable for CHIKV transmission and a shorter duration of transmission in southern coastal British Columbia, and much lower risk for the rest of Canada compared to the RCP8.5 scenario. However, if the agreement fails, Canada will be on track for the RCP8.5 path, and the RCP8.5 projections will be the most likely.

While our findings are not surprising given the small number of cases of autochthonous transmission of CHIKV in North America, our study is the first to quantify the risk of CHIKV transmission in Canada in terms of when, where, and for how long transmission may occur, which is useful for forming public health policy. Furthermore, this study shows where northern/southern temperature regions will likely be under different climate projections, this is particularly useful for indicating where the borderline for exotic vector-borne pathogens transmitted by *Ae. albopictus* will likely be under climate change.

The work presented in this study could have implications for other mosquito-borne pathogens sharing the same vectors as CHIKV. At the time of writing, the outbreak of Zika virus (ZIKV) in the Americas and the Caribbean was causing concern due to the potential for returning Canadian travelers to spread the disease in the susceptible Canadian population (Fonseca et al. 2014; Musso et al. 2016; Petersen et al. 2016). ZIKV is an emerging disease transmitted by *Ae. aegypti*, *Ae. albopictus* mosquitoes and other *Aedes* spp. mosquitoes (Grard et al. 2014; Ledermann et al. 2014; Musso et al. 2014; Musso and Gubler 2016; Petersen et al. 2016). With additional data input specific to ZIKV such as the relationship between temperature and the EIP of ZIKV in the vectors, and the duration of the human ZIKV viraemia, the research presented here could be updated rapidly to assess the climatic suitability for autochthonous mosquito-borne ZIKV transmission in Canada. We do not currently have ZIKV-specific transmission parameters, but given that the epidemiology of ZIKV is similar to CHIKV and dengue, they are transmitted by the same vectors and they appear to co-circulate (Campos et al. 2015; Cao-Lormeau and Musso 2014; Musso and Gubler 2016), it is likely that Canada is currently not climatically suitable for autochthonous mosquito-borne ZIKV transmission, nor would we expect the risk for transmission to increase significantly with short-term and long-term projected climate. This conclusion is not surprising given ZIKV (and CHIKV) have historically been restricted to tropical and subtropical biomes (Petersen et al. 2016; Weaver and Lecuit 2015). This does not preclude autochthonous ZIKV transmission in Canada via secondary transmission routes such as sexual transmission; which was first reported in April 2016 (Public Health Agency of Canada 2016). Similar to our risk assessment for CHIKV, we cannot rule out other competent ZIKV vectors that may already be established in Canada. Routine surveillance of ZIKV and potential ZIKV vectors should be considered in southern Ontario, Québec, the Canadian Prairies, and southern coastal British Columbia.

There are a number of limitations in this quantitative risk assessment; one of the main assumptions is that climatic conditions can accurately identify suitable habitat for vectors and thus classify risk areas for mosquito-borne diseases. This does not account of the possibility that vectors evolve over time and that changes in their distribution may not be exclusively linked to climatic conditions (Fischer et al. 2014). Although there are many other factors that contribute to the overall risk, ecological risk is considered a primary driver for where CHIKV transmission may occur and climate-driven species distribution models, including models for *Ae. albopictus*, have been shown to predict the distribution of mosquitoes and the diseases that they can transmit with acceptable accuracy in a public health context (Brady et al. 2014; Caminade et al. 2012; European Center for Disease Prevention and Control 2009; Fischer et al. 2011; Ogden et al. 2014). Our study focused on climatic conditions during the warmest months of the year in Canada because they present the highest risk for virus transmission; however, as travel to CHIKV-affected countries by Canadians peak in winter (Statistics Canada 2016), the risk of viraemic travelers returning to Canada during the summer is lower. The impact of this reduced risk was not explored in this study because we focused on the ecological risk factors essential for CHIKV transmission rather than behavioral factors, but risk for autochthonous CHIKV transmission in Canada is likely influenced by this factor. We also calculated mean monthly temperature (T_{mean}) by averaging the mean daily maximum and mean daily minimum temperatures together rather than take into account of the daily temperature ranges. Our calculation of T_{mean} does not take into account of the sensitivity to temperature extremes of *Ae. albopictus* egg survival over a short period of time (Thomas et al. 2012) nor how daily temperature fluctuations might impact other aspects of their life cycle as observed in *Ae. aegypti* (Carrington et al. 2013), thus our risk maps based on T_{mean} may overestimate the risk for CHIKV transmission. Another limitation is that this study only considers how changes in climate may affect future CHIKV transmission risk in Canada, it does not consider other factors that may influence the future risk such as advances in medicine (development of a CHIKV vaccine or effective treatment for CHIKV), changes in socioeconomic, demographic, and population factors that influence human exposure and changes in human behavior relating to climate change such as spending more time outdoors or indoors. Although future changes in these factors cannot be projected, it is likely they will have an impact on the possibility of CHIKV transmission in Canada in the future.

There are some data quality issues in this study. Data inputs for the CHIKV transmission model were based on very few CHIKV studies to date with some substitution of dengue data for CHIKV given the similarities between the epidemiology of the two viruses, their shared vectors and cocirculation (Campos et al. 2015; Cao-Lormeau and Musso 2014; Musso and Gubler 2016). There are few field estimates of biting rates and the numbers of mosquitoes per human, and how human behaviors and interventions (mosquito avoidance, mosquito control), infrastructure and environment in Canada (where the majority of Canadians live in an urbanized setting, i.e., air-conditioned homes, lack of stagnant water) affect these is unknown. We also do not have precise information on where Canadian travelers might be returning home from CHIKV-affected countries. However, we used a stochastic model, drawing from a range of probability distributions that were informed by a recent and comprehensive scoping review (S. Garasia et al. unpublished data, 2016) to account for uncertainty in the input parameters. Sensitivity analysis indicate risk maps produced using the 75th percentile R_0 values did not significantly change the conclusions using the mean R_0 values, and the model outputs are reasonable when compared to the temperature limits of historical CHIKV outbreaks and *Ae. albopictus* survival in other countries (Brady et al. 2013; Fischer et al. 2013; Lumsden 1955; Tilston et al. 2009). We ran an additional sensitivity analysis (not presented) to modify the EIP at 28°C from a mean of 6 days to a mean of 5 days given the temperature-EIP relationship for CHIKV is not well understood and may be shorter than for DENV. We found that the temperature range corresponding to R_0 values were very similar to those using the 75th percentile R_0 values, thus a shorter EIP is expected to increase the distribution and duration of CHIKV transmission in Canada. Also, there are uncertainties regarding the climatic limits for, and current distribution of, *Ae. albopictus* that requires further study (Ogden et al. 2014).

Data quality issues with the climate models used include uncertainty in climate scenarios from one single model and one bias correction approach used to drive the models, and only using data up until 2010. As the risk maps do not incorporate the five most recent years of climate data, the current risks identified is likely an underestimation of the risk given the climate in Canada over the last 5 years has been systematically warmer in the majority of the country compared to previous decades (1980s and 1990s) and climate baseline (Government of Canada 2016). Although the climate data from the bias-corrected models in this study were not far outliers compared to other RCMs and did not deviate significantly from the ensemble mean (see Figure S1), we note that over the summer months the models predicted higher temperatures and drier summers than the ensemble mean. The former is likely to result in a conservative estimate in the risk maps, whereas the latter may result in the under-prediction of the suitability for *Ae. albopictus*. Future research is needed to explore the impact of variations in climate model outputs on projected distributions by using model ensembles (IPCC 2013).

With the data we have at present, the current risk of autochthonous CHIKV transmission in Canada appears to be very low, and risk is restricted to very small parts of Canada under short-term and long-term projected climate. While our findings are not surprising, our study is the first to quantify the risk of CHIKV transmission in Canada which is useful for forming public health policy by identifying the risk of incursion of exotic vector-borne pathogens that are currently endemic to tropical and subtropical regions, into countries at high latitudes with climate change. This study identifies that southern Canada may be the very northern limit for transmission of these pathogens with climate change. Other factors need to be explored however, which include understanding when and where Canadian travelers are likely to return, infrastructure in Canada that may support vector populations in what would be expected to be climatically unsuitable regions, and whether or not there are other competent vectors in Canada. Further research to close the gap on our current understanding of CHIKV and CHIKV vectors, improved surveillance on *Ae. albopictus* in North America, and enhanced climate projection models (using model ensembles) will allow us to better predict the current and future risk of transmission of CHIKV and other exotic vector-borne pathogens in Canada.

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